Stress and glucocorticoids promote oligodendrogenesis in the adult hippocampus.

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Public Summary:
Stress can exert long-lasting changes on the brain that contribute to vulnerability to mental illness, yet mechanisms underlying this long-term vulnerability are not well understood. We hypothesized that stress may alter the production of oligodendrocytes in the adult brain, providing a cellular and structural basis for stress-related disorders. We found that immobilization stress decreased production of neurons and increased the production of olidgodendrocytes from neural stem cells in the hippocampus of the adult brain. This effect could be replicated by injection of the stress hormone corticosterone. Hippocampal neural stem cells grown in tissue culture in the presence of corticosterone showed increased expression of genes characteristic of oligodendrocytes, consistent with the in vivo findings. These results suggest that stress may alter hippocampal function by promoting oligodendrogenesis, thereby altering the cellular composition and white matter structure.

Scientific Abstract:
Stress can exert long-lasting changes on the brain that contribute to vulnerability to mental illness, yet mechanisms underlying this long-term vulnerability are not well understood. We hypothesized that stress may alter the production of oligodendrocytes in the adult brain, providing a cellular and structural basis for stress-related disorders. We found that immobilization stress decreased neurogenesis and increased oligodendrogenesis in the dentate gyrus (DG) of the adult rat hippocampus and that injections of the rat glucocorticoid stress hormone corticosterone (cort) were sufficient to replicate this effect. The DG contains a unique population of multipotent neural stem cells (NSCs) that give rise to adult newborn neurons, but oligodendrogenic potential has not been demonstrated in vivo. We used a nestin-CreER/YFP transgenic mouse line for lineage tracing and found that cort induces oligodendrogenesis from nestin-expressing NSCs in vivo. Using hippocampal NSCs cultured in vitro, we further showed that exposure to cort induced a pro-oligodendrogenic transcriptional program and resulted in an increase in oligodendrogenesis and decrease in neurogenesis, which was prevented by genetic blockade of glucocorticoid receptor (GR). Together, these results suggest a novel model in which stress may alter hippocampal function by promoting oligodendrogenesis, thereby altering the cellular composition and white matter structure.Molecular Psychiatry advance online publication, 11 February 2014; doi:10.1038/mp.2013.190.